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EXAMINER				
SISSON, BRADLEY L				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/613,903

Applicant(s)

JORDAN, HEATHER J.

Examiner

Bradley L. Sisson

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 March 2011.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 141, 150, 155-159 and 161-173 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 141, 150, 155-159 and 161-173 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 23 August 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Correspondence's Patent Drawing Review (PTO-940)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 31 March 2011 has been entered.

Drawings

2. The drawings were received on 23 August 2002. These drawings are acceptable.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

Art Unit: 1634

2. Ascertaining the differences between the prior art and the claims at issue.
 3. Resolving the level of ordinary skill in the pertinent art.
 4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
5. Claims 141, 150, 155-157, 159, 162-173 remain rejected under 35 U.S.C. 103(a) as obvious over either US Patent 5,316,908 (Carlson et al.) or Stratagene (1993) or Stratagene Catalog (1993).
6. Attention is directed to MPEP 2129 [R-6], Admissions as Prior Art, which states in part:

I. ADMISSIONS BY APPLICANT CONSTITUTE PRIOR ART

A statement by an applicant >in the specification or made< during prosecution identifying the work of another as "prior art" is an admission **>which can be relied upon for both anticipation and obviousness determinations, regardless of whether the admitted prior art would otherwise qualify as prior art under the statutory categories of 35 U.S.C. 102. *Riverwood Int'l Corp. v. R.A. Jones & Co.*, 324 F.3d 1346, 1354, 66 USPQ2d 1331, 1337 (Fed. Cir. 2003); *Constant v. Advanced Micro-Devices Inc.*, 848 F.2d 1560, 1570, 7 USPQ2d 1057, 1063 (Fed. Cir. 1988).

7. Claims 141, 165, and 169 are the only independent claims pending. Claim 141 is representative, and for convenience, is reproduced below.
8. As a result of amendment, claim 141 has been amended so to recite the clause "consisting essentially of" a plurality of double stranded nucleic acid fragments." As set forth at MPEP 2111.03:

The transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention. *In re Herz*, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976) (emphasis in original)

For purposes of examination, the claims have been construed as encompassing not only the explicitly recited nucleic acid fragments/bands, as well as any number and combinations of

additional ingredients, including alternative bands, so long as they do not affect the claimed nucleic acid fragments that go to form the claimed ladder.

9. Attention is directed to the decision in *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007):

When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

10. It is further noted that prior art is not limited to the four corners of the documentary prior art being applied. Prior art includes both the specialized understanding of one of ordinary skill in the art, and the common understanding of the layman. It includes “background knowledge possessed by a person having ordinary skill in the art. . . [A] court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.” *KSR* at 1396.

11. Suggestion, teaching or motivation does not have to be explicit and “may be found in any number of sources, including common knowledge, the prior art as a whole or the nature of the problem itself” *Pfizer, Inc. v. Apotex, Inc.* 480 F.3d 1348, 82 USPQ2d 1321 (Fed. Cir. 2007) citing *Dystar Textilfarben GMBH v. C. H. Patrick Co.*, 464 F.3d 1356 (Fed. Cir. 2006).

12. Carlson et al., Fig. 1, disclose a nucleic acid ladder that comprises multiple nucleic acid fragments that have the same intensity. As seen in the figure, below, there are 5 bands that are less than 1 kb and there are at least four bands that have greater than 1 kb in mass. Such a showing meets a limitation “wherein at least two of the plurality of nucleic acid fragments have a

size greater than 1 kb, and wherein at least two of the plurality of nucleic acid fragments have a size less than 1 kb.”

13. It is noted with particularity that a compound and its properties are inseparable. While one may identify new properties or new means for evaluating same, such does not make an old compound, or old composition, new and patentable. The claims recite no chemical or physical component that would make the nucleic acid of the claims any different from the nucleic acid ladders of the prior art. Indeed, page 8, fifth paragraph, of the specification states in part: “However, any nucleic acid molecule or combination of molecules may be used to produce the ladders or compositions of the invention.”

14. While Fig. 1 is a drawing and not a photograph, the specification does state that the Figure does represent the migration of the nucleic acid ladder in an electrophoretic environment. Said Figure clearly shows that the bands have the same relative intensity.

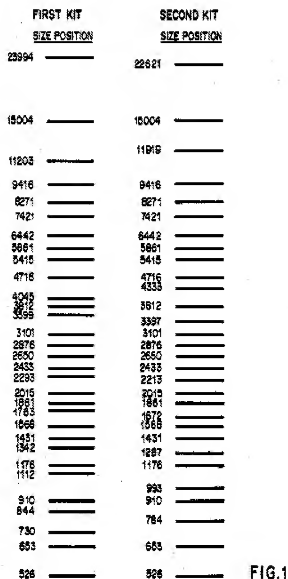


FIG.1

15. To the extent that claim 159 does positively recite that the ladder is stained with ethidium bromide, it is noted that Carlson et al., disclose such at column 4. For purposes of examination, ethidium bromide is construed to meet the requirements of a dye as it is typically used to stain the entire gel, and with it, stain (dye) preferentially the nucleic acids therein. Accordingly, a limitation of claims 157, 159, and 160 is deemed to be met by the disclosure of Carlson et al.

16. Carlson et al., disclose nucleic acid ladders that comprise numerous bands that span a wide range of fragment sizes. While some of the rungs of the nucleic acid ladder fall within the recited ranges of claims, the disclosed nucleic acid ladders also comprise additional nucleic acid fragments that are outside of the recited range. Such additional bands do not detract from the instant rejection as the claims, through the use of the term “consisting essentially of,” (claim 141, line 1) or “comprising” (claim 165, line 1; and claims 169, line 1) allows for the inclusion of additional reagents (rungs of a ladder), even in significant amounts.

17. The claims do not recite any material difference in the composition of nucleic acid individual fragments. While claim 141 does require that the “relative mass” of the different fragments “is no more than 3 time [*sic*, times] the relative mass of any other fragment of the plurality,” such is deemed to be effectively represented by FIG. 1 which shows that the bands all have the same relative intensity.

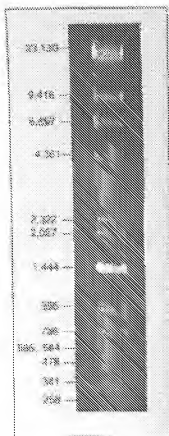
18. While newly presented claims have language directing to how the relative mass is to be calculated, it is noted that the instant claims are drawn to a composition, not to a method. Accordingly, the same composition, defined by other terms, can and does anticipate the claimed invention. In support of this position, attention is directed to page 6 of the disclosure which states in part:

Preferably, the relative mass of each different sized fragment is substantially equivalent such that discrete bands of substantially equal intensity are produced when the fragments are resolved on a gel and stained.

19. Stratagene, at page T22, disclose a Lambda/Hind III nucleic acid ladder. As seen in the image, the ladder comprises multiple fragments that appear to have “substantially equal

intensity.” The ladder clearly comprises at least two fragments larger than 1 kb and two fragments less than 1 kb which have “substantially equal intensity.” Given that a compound and its properties are inseparable, and given applicants statement that nucleic acid fragments that have “substantially equivalent intensities” also have substantially equivalent relative mass (*supra*), the fragments of Stratagene are deemed to anticipate the claimed nucleic acid ladder.

20. To the degree that claims 150, 155, 156, 165-172 define alternative ranges of the fragment sizes, the nucleic acid fragments of Stratagene clearly fall within each of the stated ranges. Accordingly, the DNA ladder of Stratagene is deemed to meet a limitation of each of said claims.



21. The selection of which band or combination of bands, and their relationship to one another, is not deemed to constitute a patentable distinction over the prior art. Rather, such limitations are deemed to be the result of design choice and/or routine optimization.
22. It is well settled that routine optimization is not patentable, even if it results in significant improvements over the prior art. In support of this position, attention is directed to the decision in *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955):

Normally, it is to be expected that a change in temperature, or in concentration, or in both, would be an unpatentable modification. Under some circumstances, however, changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art. In *re Dreyfus*, 22 C.C.P.A. (Patents) 830, 73 F.2d 931, 24 USPQ 52; In *re Waite et al.*, 35 C.C.P.A. (Patents) 1117, 168 F.2d 104, 77 USPQ 586. Such ranges are termed "critical" ranges, and the applicant has the burden of proving such criticality. In *re Swenson et al.*, 30 C.C.P.A. (Patents) 809, 132 F.2d 1020, 56 USPQ 372; In *re Scherl*, 33 C.C.P.A. (Patents) 1193, 156 F.2d 72, 70 USPQ 204. However, even though applicant's modification results in great improvement and utility over the prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art. In *re Sola*, 22 C.C.P.A. (Patents) 1313, 77 F.2d 627, 25 USPQ 433; In *re Normann et al.*, 32 C.C.P.A. (Patents) 1248, 150 F.2d 708, 66 USPQ 308; In *re Irmischer*, 32 C.C.P.A. (Patents) 1259, 150 F.2d 705, 66 USPQ 314. More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. In *re Swain et al.*, 33 C.C.P.A. (Patents) 1250, 156 F.2d 239, 70 USPQ 412; *Minnesota Mining and Mfg. Co. v. Coe*, 69 App. D.C. 217, 99 F.2d 986, 38 USPQ 213; *Allen et al. v. Coe*, 77 App. D. C. 324, 135 F.2d 11, 57 USPQ 136. (Emphasis added)

23. The plurality of bands that make up each rung in the ladder of *Carlson et al.*, and of *Stratagene* are deemed to have "substantially relative equal mass" as the band is shown to have "substantially equal intensities" after being separated as bands on a gel and stained. Accordingly, claims 141, 150, 155-157, 159, 162-173 remain rejected under 35 U.S.C. 103(a) as obvious over either US Patent 5,316,908 (*Carlson et al.*) or *Stratagene* (1993) or *Stratagene Catalog* (1993).

24. Claim 158 remains rejected under 35 U.S.C. 103(a) as being unpatentable over either US Patent 5,316,908 (Carlson et al.) or Stratagene (1993) or Stratagene Catalog (1993) when taken in view of US Patent 5,635,365 (Ansari et al.).
25. See above for the basis of the rejection as it relates to the disclosure of both Carlson et al., and Stratagene.
26. Neither Carlson et al., nor Stratagene have been found to disclose staining the ladders with SYBR green ([2-[N-(3-dimethylaminopropyl)-N-propylamino]-4-[2,3-dihydro-3-methyl-(benzo-1,3-thiazol-2-yl)-methylidene]-1-phenyl-quinolinium]⁺).
27. Ansari et al., column 15, third paragraph, teaches explicitly of staining a gel with SYBR green so to enable visualization of the nucleic acid fragments separated therein.
28. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the nucleic acid ladders of either Carlson et al., or Stratagene with SYBR green as disclosed by Ansari et al., as such would have allowed the ordinary artisan with an easy, sensitive and reproducible means for detecting nucleic acids. In view of the detailed teachings in the prior art, said ordinary artisan would have had a most reasonable expectation of success.
29. For the above reasons, and in the absence of convincing evidence to the contrary, claim 158 remains rejected under 35 USC 103(a) as being unpatentable over either US Patent 5,316,908 (Carlson et al.) or Stratagene (1993) or Stratagene Catalog (1993) when taken in view of US Patent 5,635,365 (Ansari et al.).

Response to argument

30. At page 7, bridging to page 8, of the response of 31 March 2011, applicant's representative asserts that the teachings of the prior art are not relevant as one of the figures relied upon is a graphic representation and not an actual picture.

31. The above argument has been considered and has not been found persuasive. It is noted that applicant has not indicated how anything about the illustration is technically flawed or that the conclusions drawn therefrom cannot be sustained by the teachings of the prior art. Further, applicant's representative has not cited any legal precedent that bars the use of drawings as evidence.

32. Applicant's representative, at page 8 of the response, asserts:

Applicant respectfully submits that it is improper to extrapolate information relating to the mass of individual bands using Fig. 1, since the intent thereof was to represent band migration (i.e., band size), not mass (i.e., DNA content). (Emphasis in the original)

The above arguments have been considered and have not been found persuasive. It is noted that applicant has not shown how the different bands, or rungs in the metaphorical ladder, do not have a different mass, or show how the mass of the bands changes in direct relationship to the number of nucleotides. Indeed, a compound and its properties are inseparable. Just as the addition of nucleotides makes the molecule longer, it also increases its mass.

33. Applicant's representative, at page 8 of the response, asserts:

As previously discussed, the very nature by which Carlson's DNA markers are made (i.e., by pooling restriction digests of a single larger L-page DNA) will not result in a DNA marker ladder shown in Fig. 1. Carlson clearly states "[t]he ladder is made up of pooled DNA restriction endonuclease digests" (Abstract).

The above argument has been considered and has not been found persuasive as the claimed composition is not claimed as a product-by-process, wherein the process is materially different, and/or results in a product that is materially different from that disclosed in the prior art. Indeed, the claimed composition may very well be manufactured by a process of pooled DNA fragments as there is no limitation that precludes such from being done.

34. The prior art has clearly disclosed the generation and use of nucleic acid ladders. The selection of one or more concentrations of individual members of the nucleic acid ladder is deemed to be routine optimization and/or a design choice. A review of the disclosure fails to find where any unexpected property/result is obtained.

35. At page 9 of the response argument is presented that the depiction in Carlson's FIG. 1 is inconsistent with the method disclosed in the specification and as such, Carlson et al., do not teach or render obvious a nucleic acid ladder that has the claimed mass relationships.

36. The above argument has been considered and has not been found persuasive, as it is without dispute that Carlson et al., through their FIG. 1, do teach a nucleic acid ladder where the bands are depicted as having the same relative mass, and therein meeting a limitation of the claims. It is noted that the claimed invention is directed to a product and not to a process or a product-by-process. While Carlson may well arrive at one embodiment of the ladder by the pooling of different nucleic acid fragments, the mechanism or method used to arrive at any given pooling speaks to a method, and not to the product. As noted above, the claimed invention is not directed to a method of producing a product, but rather, to a product. Accordingly, it matters not what method or combination of methods, known in the prior art at the time of filing, could be used to generate the product so long as the product is achieved. Carlson et al., have amply

disclosed the claimed nucleic acid ladder. The aspect that the may have arrived with the product through means different from that of applicant, and/or that applicant has been unable to reproduce the result of Carlson et al., does not take away from Carlson et al., teaching the claimed product.

37. At page 10 of the response argument is made that one of the bands depicted by Carlson et al., actually has 2.6 times the mass of another band.

38. While not conceding to the point raised by applicant's representative, it is noted that claim 141 allows for such variance. Indeed, the nucleic acid ladder of claim 141 explicitly encompasses embodiments where "the relative mass of any one fragment of the plurality is no more than 3 time the relative mass of any other fragment of the plurality."

39. Even if one were to assert that there was a band of Carlson et al., that was outside the range of 3x the mass of any other nucleic acid band, such would not overcome the aspect that one of skill in the art, at the time of filing, could select and design a nucleic acid ladder of their own choosing as such is a matter of an obvious design choice.

40. For the above reasons, and in the absence of convincing evidence to the contrary, the rejections are maintained.

Conclusion

41. Objections and/or rejections which appeared in the prior Office action and which have not been repeated hereinabove have been withdrawn.

42. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art

of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

43. A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

44. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L. Sisson whose telephone number is (571)272-0751. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

45. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

46. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bradley L. Sisson/
Primary Examiner, Art Unit 1634